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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/867,159	05/29/2001	Emile Loria	01-346	5964

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/867,159	LORIA ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 March 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *03 March 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☐ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *None*.

Claim(s) objected to: *None*.

Claim(s) rejected: *1-4, 10-18, 26-28 and 30-35*.

Claim(s) withdrawn from consideration: *5-9 and 19-25*.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Continuation of 3. Applicant's reply has overcome the following rejection(s): The rejection of claim 29 under 35 USC 112 second paragraph is hereby withdrawn in view of canceling claim 29.

Continuation of 5. does NOT place the application in condition for allowance because: Deleting the term "at galenic level" in claim 3 does not overcome the rejection under 35 USC 112 second paragraph because claim 3 still recites "the anti-allergic pharmaceutical compsotion..., enabling release of peptides and other chemical substance in independent manner". There is a lack of antecedent basis for "peptides and other chemical substances" in base claim 1 or claim 2. All rejections remain. Applicant's arguments have been fully considered but not found convincing for the same reasons set forth in Office Action mailed 9/2/03. Applicant argues that the present invention is anti-allergic pharmaceutical composition contains at least active agents chosen from among (i) one allergen; (ii) one antihistamine compound, and (iii) one inhibitor of histamine synthesis. However, the specific allergen, the specific anti-histamine compound and the specific inhibitor of histamine synthesis are not recited in the claims. Further, merely deleting claim 29 and deleting the term "galenic level" in claim 3 does not address the issues of enablement, written description, and the art rejections.

With respect to the enablement rejection of claims 1-4, 10-18, 26-28 and 30-35 under 35 U.S.C. 112, first paragraph, the scope of the claims is drawn to any anti-allergic pharmaceutical composition comprising at least two of any allergen, any antihistamine compound or any inhibitor of histamine synthesis. The specification discloses only two allergens from dust mite of D. Pteronyssinus (DP) comprising SEQ ID NO: 1 and D. Farinae (DF) comprising SEQ ID NO: 2 (page 5). The specification further discloses three allergen peptides wherein the peptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NOS: 3-5 that are derived from the cysteine protease of dust mite D. Pteronyssinus (DP) of SEQ ID NO: 1 and D. Farinae (DF) (See page 6). The specification discloses a pharmaceutical composition comprising (i) allergen peptide mentioned above, (ii) an antihistamine compound such as the ones recited in claim 10 and (iii) tritoqualine which is a histamine synthesis inhibitor and a histidine decarboxylase inhibitor and (iv) a pharmaceutical acceptable vehicle (page 10-11) for induction of tolerance to dust mite and to block the histamine synthesis, which is the terminal phase of allergy. The terms "antihistamine compound", "allergen" and "inhibitor of histamine synthesis" have no structure without the specific amino acid sequence, or chemical structure. Given the indefinite number of undisclosed allergens, anti-histamine compound and inhibitors, there is insufficient guidance as to the structure of any "allergen", "antihistamine compound" and "inhibitors of histamine synthesis", let alone which undisclosed "compound" or "inhibitor" has the desired function, in turn, would be useful for the claimed pharmaceutical composition. Further, there is inadequate in vivo working example demonstrating all undisclosed compound have anti-histamine effect or inhibits histamine synthesis. Stryer et al teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages). Ngo et al teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions could result in substantially different pharmacological activities. Fasler et al teach that peptides derived from house dust mite Der p1 are modified by even a single amino acid substitutions at positions 173, 175, 176, 180 and 181 with alanine or glycine failed to induce Der p1 specific T cell proliferation and IL-2, IL-4 and IFN-g production. Fasler et al further teach that substituting a neutral amino acid residue such as Asn at position 173 with either a basic Lysine, which is a hydrophobic amino acid residue did not induce T cell proliferation and cytokine production. However, substitution amino acid positions other than 173, 175, 176, 180 and 181 induces normal or only slightly reduced proliferative responses and cytokine production by T cells (page 524, in particular). Without the specific amino acid sequence of allergen (claims 1, and 14), the major antigens of acarids (claim 4), the chemical structure of antihistamine compound and the inhibitor of histamine synthesis (claims 1-3, 11, 15-18), it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

With respect to the written description rejection of claims 1-4, 10-18, 26-28 and 30-35 under 35 U.S.C. 112, first paragraph, the scope of the claims is drawn to any anti-allergic pharmaceutical composition comprising at least two of any allergen, any antihistamine compound or any inhibitor of histamine synthesis. The specification discloses only two allergens from dust mite of D. Pteronyssinus (DP) comprising SEQ ID NO: 1 and D. Farinae (DF) comprising SEQ ID NO: 2 (page 5). The specification further discloses three allergen peptides wherein the peptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NOS: 3-5 that are derived from the cysteine protease of dust mite D. Pteronyssinus (DP) of SEQ ID NO: 1 and D. Farinae (DF) (See page 6). The specification discloses a pharmaceutical composition comprising (i) allergen peptide mentioned above, (ii) an antihistamine compound such as the ones recited in claim 10 and (iii) tritoqualine which is a histamine synthesis inhibitor and a histidine decarboxylase inhibitor and (iv) a pharmaceutical acceptable vehicle (page 10-11) for induction of tolerance to dust mite and to block the histamine synthesis, which is the terminal phase of allergy. The terms "antihistamine compound", "allergen" and "inhibitor of histamine synthesis" have no structure without the specific amino acid sequence, or chemical structure. Given the indefinite number of undisclosed allergens, anti-histamine compound and inhibitors, there is insufficient guidance as to the structure of any "allergen", "antihistamine compound" and "inhibitors of histamine synthesis", let alone which undisclosed "compound" or "inhibitor" has the desired function, in turn, would be useful for the claimed pharmaceutical composition. Other than the specific allergen peptides, and the specific inhibitor of histamine synthesis, there is inadequate written description about the structure associated with function of all active agent such as (1) all allergen, all major antigens, any mixture of all major antigens of acarids, (2) all "antihistamine compound", (3) all "inhibitor of histamine synthesis", all "inhibitor of histidine decarboxylase" for treating any allergy, much less to "prevent" any allergy. Since all the allergen, antihistamine compound, inhibitor of histidine synthesis and inhibitor of histidine decarboxylase are not adequately described, it follows any pharmaceutical composition comprising said undisclosed allergen, antihistamine compound, inhibitor of histidine synthesis and inhibitor of histidine decarboxylase are not adequately described.

With respect to Claims 1-4, 14, 26-28 and 30-33 rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No 6,455,686 (Sept 2002, PTO 892), applicant argues that the '686 patent does not teach or suggest the subject matter. The '686 patent teaches

identification of proteins especially to D Farinae, and their use in diagnostic ro therapeutic techniques. In response, the '686 patent teaches an anti-allergic pharmaceutical composition comprising an allergen such as high molecular weight Dermatophagoides farinae proteins from mite in conjunction with other compound such as anti-histamines (column 42, lines 40-59, in particular) associated with a pharmaceutical acceptable vehicle such as phosphate buffered saline (PBS, see column 44, line 63 bridging column 45, line 1, in particular) in a controlled released formulation such as liposome, transdermal delivery systems, or osmotic pumps (See column 41, lines 20-33, in particular). The reference whole dust mite allergen from Dermatophagoides farinae inherently contains the major antigens of acrid which is capable of induce an immune reaction such as immediate hypersensitivity response (See column 51, Table 2, lines 13-15, in particular). The reference pharmaceutical composition contains from about 0.5 ng to about 1 g per kg body weight (See column 42, lines 26-28, in particular). The '686 patent further teaches a composition comprising anti-inflammatory agent or compound such as peptides from IgE or IgE specific Fc receptors or antibodies capable of binding to IgE and blocks IgE binding to Fc receptors that drive immunoglobulin heavy class switching from IgE to IgG which inherently switch from Th2 to Th1 that reduce IgE synthesis in the upstream phase while the reference anti-histamine inhibits the histamine release in the down stream phase (See column 42, lines 45-49, in particular). The reference pharmaceutical composition is administered in form of subcutaneous, intradermal, intravenous, nasal, oral, transdermal and intramuscular routes (See column 42, lines 35-39, in particular). The reference pharmaceutical composition is useful to treat allergic hypersensitivity reactions to dust mite such as allergic asthma, allergic rhinitis, atopic and allergic eczema or to desensitize humans who are allergic to dust mite (See column 36, lines 31-36, column 42, lines 60-63, in particular). The reference pharmaceutical composition contains a quantity of 1 x 10-8 microgram to about 100 mg or from about 1x 10-7 mg to about 10 mg (See column 27, lines 31-34, in particular). Claim 14 is included in this rejection because the claimed limitations of 1 to 1500 mg or from 10 to 150 mg include the reference quantity of allergy. Thus, the reference teachings anticipate the claimed invention.

With respect to Claims 1-4, and 10-13, 15-18 and 34-35 rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 6,455,686 (Sept 2002, PTO 892) in view of US Pat No 4,302,458 (Nov 1981, PTO 892) and US Pat No 6,258,816 (July 2001, PTO 892) or US Pat No. 5,827,852 (Oct 1998, PTO 892) or US Pat No 6,319,513 (Nov 2001, PTO 892), applicant argues that none of the partents teach or suggest the combination of compounds set forth in claim 1. None of the cited and applied references describes the fact of simultaneously inhibiting the synthesis of histamine and competing histamine fixation. However, claim 1 merely recites an anti-allergic pharmaceutical composition containing at least two active agents chosen among (i) one allergen, (ii) one antihistamine compound, (iii) one inhibitor of histamine synthesis, said active agents being associated in said composition with a pharmaceutically acceptable vehicle. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e.,simultaneously inhibiting the synthesis of histamine and competing histamine fixation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

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